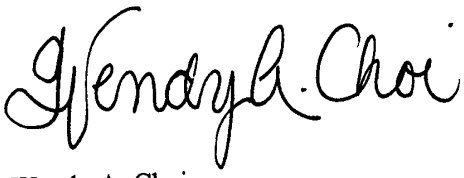
REMARKS

Applicants submit that the amendment to the claims does not introduce new matter and are fully supported by the specification and claims as originally filed. Applicants submit that the present claims meet all the requirements for patentability. The Examiner is respectfully requested to allow all the present claims. If the Examiner is of a contrary view, the Examiner is requested to contact the undersigned attorney at (215) 557-3861.

Attached hereto is a marked-up version of the changes made to the specification and the claims by the current amendment. The attached page is captioned "Version with Markings to Show Changes Made."

Respectfully submitted,



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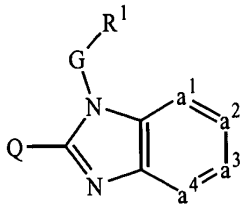
VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

1. A compound of formula



(I)

a prodrug, N-oxide, addition salt, quaternary amine, metal complex or stereochemically isomeric form thereof wherein

$-a^1=a^2-a^3=a^4-$ represents a bivalent radical of formula

-CH=CH-CH=CH- (a-1);

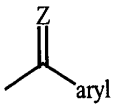
-N=CH-CH=CH- (a-2);

-CH=N-CH=CH- (a-3);

-CH=CH-N=CH- (a-4); or

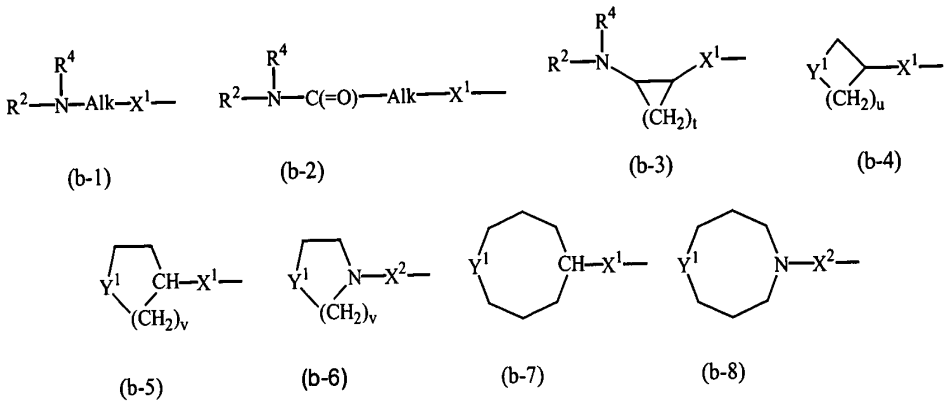
-CH=CH-CH=N- (a-5);

wherein each hydrogen atom in the radicals (a-1), (a-2), (a-3), (a-4) and (a-5) may optionally be replaced by halo, C_{1-6}alkyl, nitro, amino, hydroxy, C_{1-6}alkyloxy, polyhaloC_{1-6}alkyl, carboxyl, aminoC_{1-6}alkyl, mono- or di(C_{1-4}alkyl)aminoC_{1-6}alkyl, C_{1-6}alkyloxycarbonyl, hydroxyC_{1-6}alkyl, or a radical of formula



wherein =Z is =O, =CH-C(=O)-$NR^{5a}R^{5b}$, $=CH_2$, =CH-C_{1-6}alkyl, =N-OH or =N-O-C_{1-6}alkyl;

Q is a radical of formula



(b-1) (b-2) (b-3) (b-4)

(b-5) (b-6) (b-7) (b-8)

wherein Alk is C_{1-6}alkanediyl;

Y^1 is a bivalent radical of formula $-NR^2-$ or $-CH(NR^2R^4)-$;

X^1 is NR^4, S, S(=O), $S(=O)_2$, O, CH_2, C(=O), $C(=CH_2)$, CH(OH), $CH(CH_3)$, $CH(OCH_3)$, $CH(SCH_3)$, $CH(NR^{5a}R^{5b})$, CH_2-NR^4 or NR^4-CH_2;

X^2 is a direct bond, CH_2, C(=O), NR^4, C_{1-4}alkyl-NR^4, NR^4-C_{1-4}alkyl;

t is 2, 3, 4 or 5;

u is 1, 2, 3, 4 or 5;

v is 2 or 3; and

whereby each hydrogen atom in Alk and the carbocycles and the heterocycles defined in radicals (b-3), (b-4), (b-5), (b-6), (b-7) and (b-8) may optionally be replaced by R^3; with the proviso that when R^3 is hydroxy or C_{1-6}alkyloxy, then R^3 can not replace a hydrogen atom in the α position relative to a nitrogen atom;

G is C_{1-10}alkanediyl substituted with one or more hydroxy, C_{1-6}alkyloxy, arylC_{1-6}alkyloxy, C_{1-6}alkylthio, arylC_{1-6}alkylthio, $HO(-CH_2-CH_2-O)_n-$, C_{1-6}alkyloxy$(-CH_2-CH_2-O)_n-$ or arylC_{1-6}alkyloxy$(-CH_2-CH_2-O)_n-$;

R^1 is a monocyclic heterocycle or aryl; said heterocycle being selected from piperidinyl, piperazinyl, pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, furanyl, tetrahydrofuranyl, thienyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, pyrazolyl, isoxazolyl, oxadiazolyl; and each heterocycle may optionally be substituted with 1 or where possible more, such as 2, 3 or 4, substituents selected from halo, hydroxy, amino, cyano, carboxy, C_{1-6}alkyl, C_{1-6}alkyloxy, C_{1-6}alkylthio, C_{1-6}alkyloxyC_{1-6}alkyl, aryl, arylC_{1-6}alkyl, arylC_{1-6}alkyloxy, hydroxyC_{1-6}alkyl, mono-or di(C_{1-}

$_{6}$alkyl)amino, mono-or di(C_{1-6}alkyl)aminoC_{1-6}alkyl, polyhaloC_{1-6}alkyl, C_{1-6}alkylcarbonylamino, C_{1-6}alkyl-SO_2-NR^{5c}-, aryl-SO_2-NR^{5c}-, C_{1-6}alkyloxycarbonyl, -C(=O)-$NR^{5c}R^{5d}$, HO(-CH_2-CH_2-O)$_n$-, halo(-CH_2-CH_2-O)$_n$-, C_{1-6}alkyloxy(-CH_2-CH_2-O)$_n$-, arylC_{1-6}alkyloxy(-CH_2-CH_2-O)$_n$- and mono-or di(C_{1-6}alkyl)amino(-CH_2-CH_2-O)$_n$;

each n independently is 1, 2, 3 or 4;

R^2 is hydrogen, formyl, C_{1-6}alkylcarbonyl, Hetcarbonyl, pyrrolidinyl, piperidinyl, homopiperidinyl, C_{3-7}cycloalkyl substituted with $N(R^6)_2$, or C_{1-10}alkyl substituted with $N(R^6)_2$ and optionally with a second, third or fourth substituent selected from amino, hydroxy, C_{3-7}cycloalkyl, C_{2-5}alkanediyl, piperidinyl, mono-or di(C_{1-6}alkyl)amino, C_{1-6}alkyloxycarbonylamino, aryl and aryloxy;

R^3 is hydrogen, hydroxy, C_{1-6}alkyl, C_{1-6}alkyloxy, arylC_{1-6}alkyl or arylC_{1-6}alkyloxy;

R^4 is hydrogen, C_{1-6}alkyl or arylC_{1-6}alkyl;

R^{5a}, R^{5b}, R^{5c} and R^{5d} each independently are hydrogen or C_{1-6}alkyl; or

R^{5a} and R^{5b}, or R^{5c} and R^{5d} taken together form a bivalent radical of formula -$(CH_2)_s$- wherein s is 4 or 5;

R^6 is hydrogen, C_{1-4}alkyl, formyl, hydroxyC_{1-6}alkyl, C_{1-6}alkylcarbonyl or C_{1-6}alkyloxycarbonyl;

aryl is phenyl or phenyl substituted with 1 or more, such as 2, 3 or 4, substituents selected from halo, hydroxy, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, polyhaloC_{1-6}alkyl, and C_{1-6}alkyloxy;

Het is pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl.

2. (amended) A compound according to claim 1, wherein -a^1=a^2-a^3=a^4- is a radical of formula (a-1) or (a-2).

3. (amended) A compound according to claim 1 [or 2] wherein R^1 is phenyl optionally substituted with halo, C_{1-6}alkyl or C_{1-4}alkyloxy; or pyridyl optionally substituted with 1 or more substituents selected from arylC_{1-6}alkyloxy, C_{1-6}alkyloxyC_{1-6}alkyl, aryl, mono- or di(C_{1-6}alkyl)amino, C(=O)-$NR^{5c}R^{5d}$, halo or C_{1-6}alkyl.

4. (amended) A compound according to [any one of] claim 1, [claims 1 to 3] wherein G is C_{1-4}alkanediyl substituted with hydroxy, C_{1-6}alkyloxy, $HO(-CH_2-CH_2-O)_n-$, C_{1-6}alkyloxy$(-CH_2-CH_2-O)_n-$ or arylC_{1-6}alkyloxy$(-CH_2-CH_2-O)_n-$.

5. (amended) A compound according to [any one of] claim 1, [claims 1 to 4] wherein Q is a radical of formula (b-5) wherein v is 2 and Y^1 is $-NR^2-$.

6. (amended) A compound according to [any one of] claim 1, [claims 1 to 5] wherein X^1 is NH or CH_2.

7. (amended) A compound according to [any one of] claim 1, [claims 1 to 6] wherein R^2 is hydrogen or C_{1-10}alkyl susbstituted with NHR^6 wherein R^6 is hydrogen or C_{1-6}alkyloxycarbonyl.

8. A compound according to claim 1 wherein the compound is [(A),(S)]-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(6-bromo-2-pyridinyl)ethoxymethyl]-1H-benzimidazol-2-amine; [(A),(S)]-N-[1-(2-aminopropyl)-4-piperidinyl]-1-[ethoxy(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine (compound 75); (±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(2-methoxyethoxy)(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine; N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-6-chloro-1-[(2-methoxyethoxy)(6-methyl-2-pyridinyl)methyl]-4-methyl-1H-benzimidazol-2-amine trihydrochloride trihydrate; [(A),(R)]-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[ethoxy(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine monohydrate; (±)-N-[1-(2-aminopropyl)-4-piperidinyl]-1-[ethoxy(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine; [(A)(S)]-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[ethoxy(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine monohydrate; (±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[ethoxy(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine; [(A),(R)]-N-[1-(2-aminopropyl)-4-piperidinyl]-1-[ethoxy(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine monohydrate; (±)-N-[1-(2-

aminoethyl)-4-piperidinyl]-1-[(6-bromo-2-pyridinyl)ethoxymethyl]-2-benzimidazol-2-amine; (±)-N-[1-(2-aminoethyl)-4-piperidinyl]-1-[(2-ethoxyethoxy)(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine; [(B),(S)] N-[1-(2-aminopropyl)-4-piperidinyl]-1-[ethoxy(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine monohydrate; (±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-3-[(2-methoxyethoxy)(6-methyl-2-pyridinyl)methyl]-7-methyl-3H-imidazo[4,5-b]pyridin-2-amine; (±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(2-ethoxyethoxy)(6-phenyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine; (±)-N-[1-(2-aminoethyl)-4-piperidinyl]-1-[(2-methoxyethoxy)(6-metyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine; (±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(6-bromo-2-pyridinyl)ethoxymethyl]-4-methyl-1H-benzimidazol-2-amine monohydrate; [(A),(R)]-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(6-bromo-2-pyridinyl)ethoxymethyl]-1H-benzimidazol-2-amine; (±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(6-bromo-2-pyridinyl)ethoxymethyl]-1H-benzimidazol-2-amine;

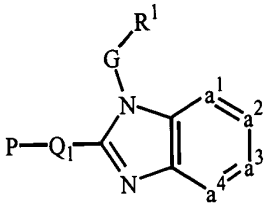
a prodrug, N-oxide, addition salt, quaternary amine, metal complex or stereochemically isomeric form thereof.

9. (amended) [A compound] A method of using as a medicine a compound as claimed in any one of claims 1 to 8 [for use as a medicine].

10. (amended) A pharmaceutical composition, comprising a pharmaceutically acceptable carrier, and as active ingredient a therapeutically effective amount of a compound as [described] claimed in any one of claims 1 to 8.

11. (amended) A process of preparing a composition as claimed in claim 10, [characterized in that,] comprising the step of intimately mixing said carrier with said compound [a pharmaceutically acceptable carrier is intimately mixed with a therapeutically effective amount of a compound as described in any one of claims 1 to 8].

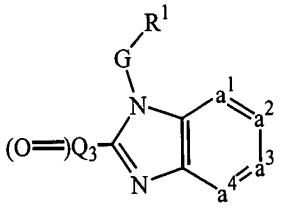
12. An intermediate of formula



(IV)

with R^1, G and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, P being a protective group, and Q_1 being defined as Q according to claim 1 provided that it is devoided of the R^2 or R^6 substituent.

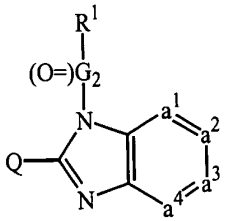
13. An intermediate of formula



(IX)

with R^1, G and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and $(O=)Q_3$ being a carbonyl derivative of Q, said Q being defined according to claim 1, provided that it is devoided of the $-NR^2R^4$ or $-NR^2-$ substituent.

14. An intermediate of formula

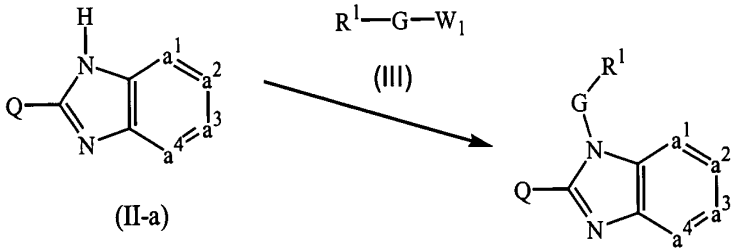


(XXII)

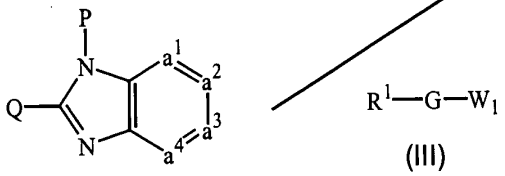
with R^1, Q and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and $(O=)G_2$ being a carbonyl derivative of G, said G being defined according to claim 1.

15. (amended) A process of preparing a compound as claimed in claim 1, [characterized by,] comprising at least one step selected from the group consisting of:

a) reacting an intermediate of formula (II-a) or (II-b) with an intermediate of formula (III)



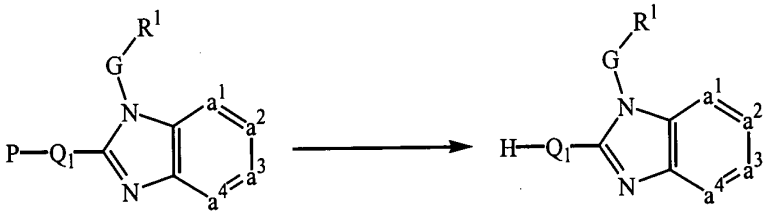
(II-a)



(II-b)

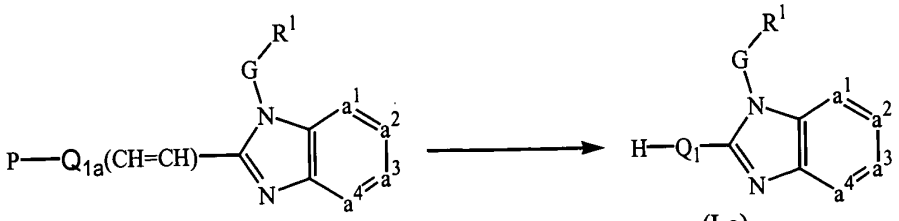
with R^1, G, Q and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and W_1 being a suitable leaving group, in the presence of a suitable base and in a suitable reaction-inert solvent;

b) deprotecting an intermediate of formula (IV)



with R^1, G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, H-Q_1 being defined as Q according to claim 1 provided that R^2 or at least one R^6 substituent is hydrogen, and P being a protective group;

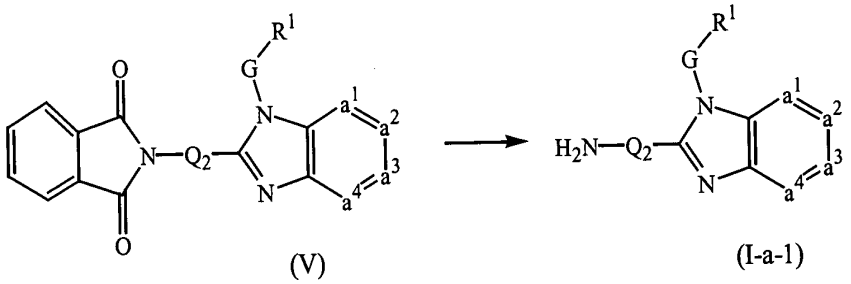
c) deprotecting and reducing an intermediate of formula (IV-a)



(IV-a) (I-a)

with R^1, G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, H-Q_1 being defined as Q according to claim 1 provided that R^2 or at least one R^6 substituent is hydrogen, Q_{1a}(CH=CH) being defined as Q_1 provided that Q_1 comprises an unsaturated bond, and P being a protective group;

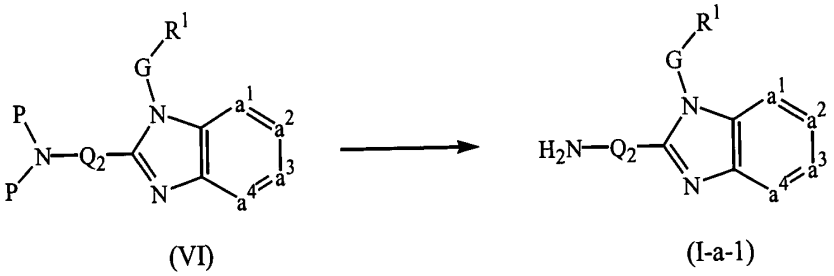
d) deprotecting an intermediate of formula (V)



(V) (I-a-1)

with R^1, G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and H_2N-Q_2 being defined as Q according to claim 1 provided that both R^6 substituents are hydrogen or R^2 and R^4 are both hydrogen;

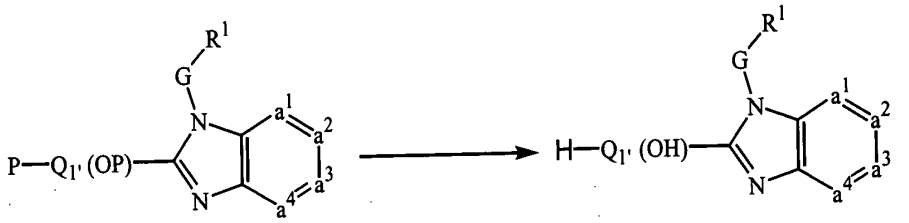
e) deprotecting an intermediate of formula (VI)



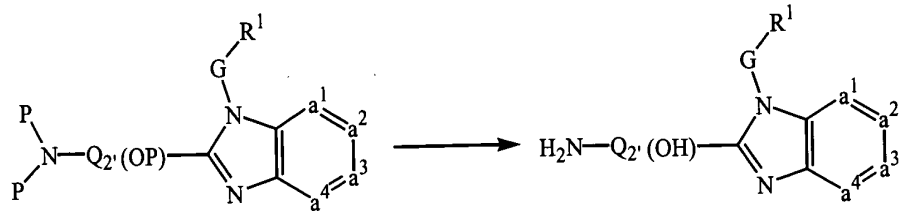
(VI) (I-a-1)

with R^1, G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and H_2N-Q_2 being defined as Q according to claim 1 provided that both R^6 substituents are hydrogen or R^2 and R^4 are both hydrogen, and P being a protective group;

f) deprotecting an intermediate of formula (VII) or (VIII)



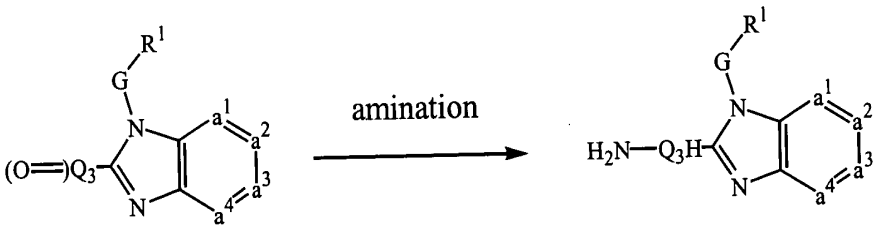
(VII) (I-a-2)



(VIII) (I-a-1-1)

with R^1, G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, $H-Q_{1'}(OH)$ being defined as Q according to claim 1 provided that R^2 or at least one R^6 substituent is hydrogen and provided that Q comprises a hydroxy moiety, $H_2N-Q_{2'}(OH)$ being defined as Q according to claim 1 provided that both R^6 substituents are hydrogen or R^2 and R^4 are both hydrogen and provided that Q comprises a hydroxy moiety, and P being a protective group;

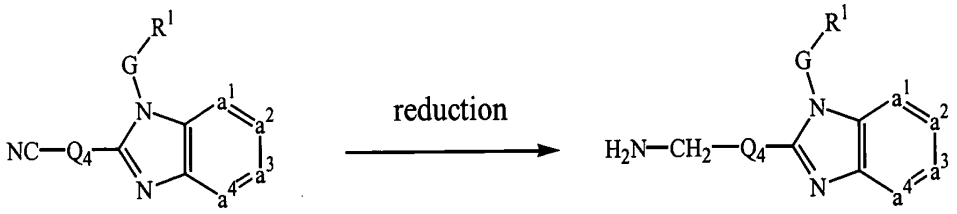
g) amination of an intermediate of formula (IX)



(IX) (I-a-1-2)

with R^1, G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and H_2N-Q_3H being defined as Q according to claim 1 provided that both R^6 substituents are hydrogen or R^2 and R^4 are both hydrogen, and the carbon adjacent to the nitrogen carrying the R^6, or R^2 and R^4 substituents contains at least one hydrogen, in the presence of a suitable amination reagent;

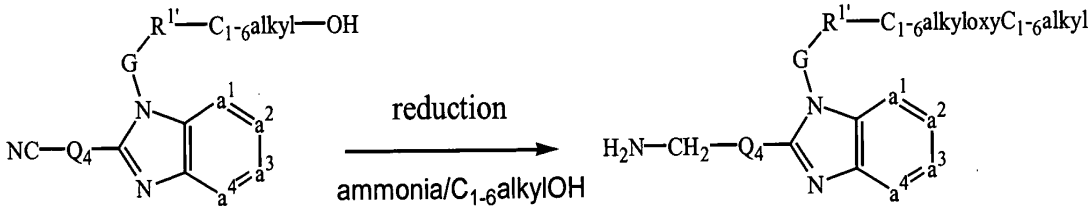
h) reducing an intermediate of formula (X)



(X) (I-a-1-3)

with R^1, G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and $H_2N-CH_2-Q_4$ being defined as Q according to claim 1 provided that Q comprises a $-CH_2-NH_2$ moiety, in the presence of a suitable reducing agent;

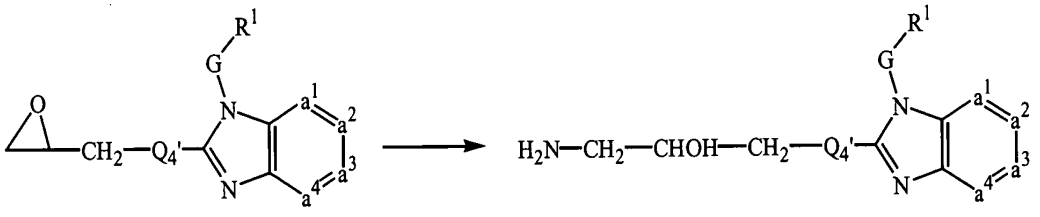
i) reducing an intermediate of formula (X-a)



(X-a) (I-a-1-3-1)

with G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, $H_2N-CH_2-Q_4$ being defined as Q according to claim 1 provided that Q comprises a $-CH_2-NH_2$ moiety, and $R^{1'}$ being defined as R^1 according to claim 1 provided that it comprises at least one substituent, in the presence of a suitable reducing agent and suitable solvent;

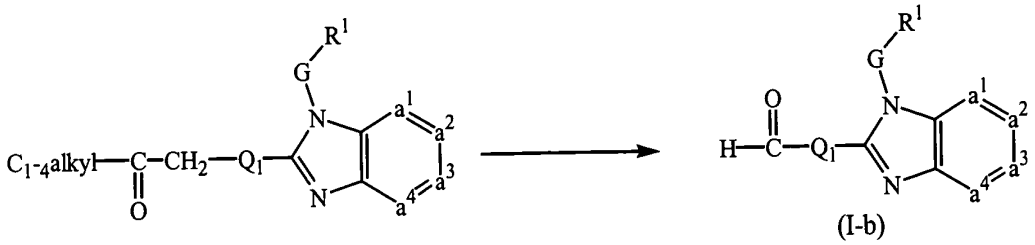
j) amination of an intermediate of formula (XI)



(XI) (I-a-1-3-2)

with R^1, G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and $H_2N-CH_2-CHOH-CH_2-Q_4$, being defined as Q according to claim 1 provided that Q comprises a $CH_2-CHOH-CH_2-NH_2$ moiety, in the presence of a suitable amination reagent;

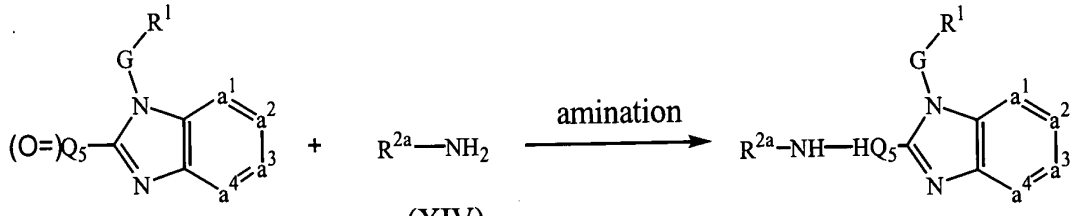
k) reacting an intermediate of formula (XII) with formic acid, formamide and ammonia



(XII) (I-b)

with R^1, G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and H-C(=O)-Q_1 being defined as Q according to claim 1 provided that R^2 or at least one R^6 substituent is formyl;

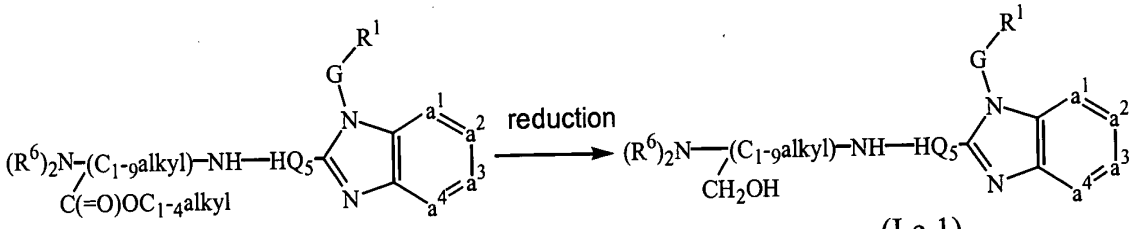
l) amination of an intermediate of formula (XIII) by reaction with an intermediate of formula (XIV)



(XIII) (XIV) (I-c)

with R^1, G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and R^{2a}-NH-HQ_5 being defined as Q according to claim 1 provided that R^2 is other than hydrogen and is represented by R^{2a}, R^4 is hydrogen, and the carbon atom adjacent to the nitrogen atom carrying the R^2 and R^4 substituents, carries also at least one hydrogen atom, in the presence of a suitable reducing agent;

m) reducing an intermediate of formula (XV)

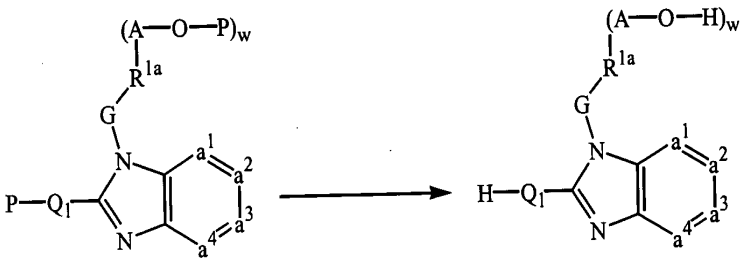


(XV) (I-c-1)

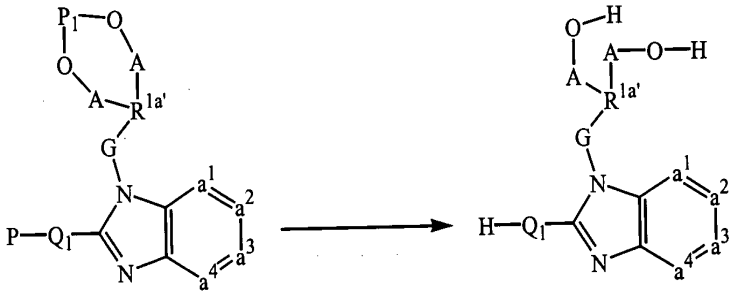
with R^1, G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and $(R^6)_2N$-[$(C_{1-9}$alkyl$)CH_2OH$]-NH-HQ_5 being defined as Q according to claim 1 provided that R^2 is other than hydrogen and is represented by C_{1-10}alkyl substituted with $N(R_6)_2$ and with hydroxy,

and the carbon atom carrying the hydroxy, carries also two hydrogen atoms, and provided that R^4 is hydrogen, and the carbon atom adjacent to the nitrogen atom carrying the R^2 and R^4 substituents, carries also at least one hydrogen atom, with a suitable reducing agent;

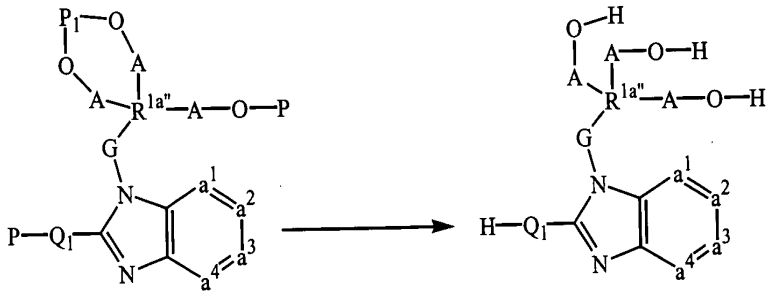
n) deprotecting an intermediate of formula (XVI), (XVI-a) or (XVI-b)



(XVI) (I-d)



(XVI-a) (I-d-1)

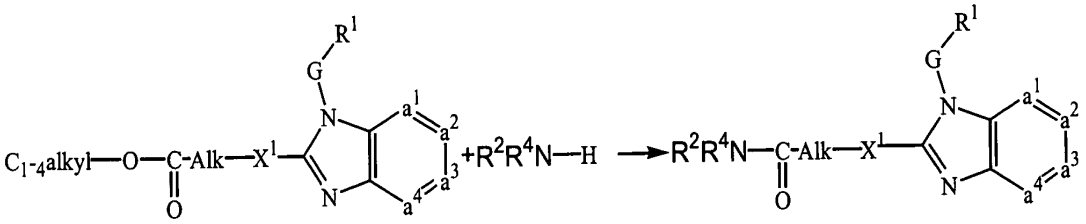


(XVI-b) (I-d-2)

with G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and $H-Q_1$ being defined as Q according to claim 1 provided that R^2 or at least one R^6 substituent is hydrogen, and R^{1a}-(A-O-H)$_w$, $R^{1a'}$-(A-O-H)$_2$ and $R^{1a''}$-(A-O-H)$_3$ being defined as R^1 according to claim 1 provided that R^1 is substituted with hydroxy, hydroxyC_{1-6}alkyl, or HO(-CH_2-CH_2-O)$_n$-,

with w being an integer from 1 to 4 and P or P_1 being a suitable protecting group, with a suitable acid[.] ;

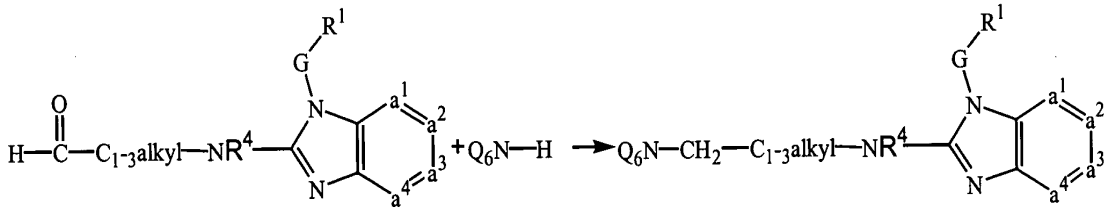
o) amination of an intermediate of formula (XVII)



(XVII) (XVIII) (I-e)

with R^1, G, $-a^1=a^2-a^3=a^4-$, Alk, X^1 R^2 and R^4 defined as in claim 1, in the presence of a suitable amination agent;

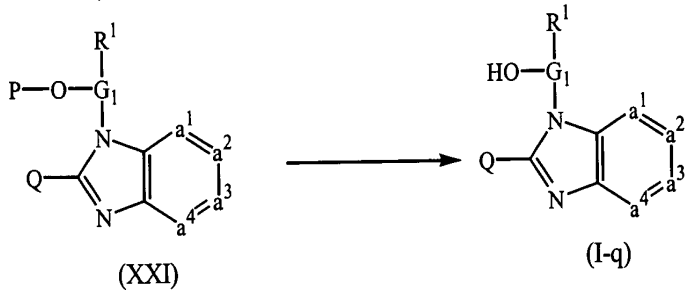
p) amination of an intermediate of formula (XIX)



(XIX) (XX) (I-p)

with R^1, G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and $Q_6N\text{-}CH_2\text{-}C_{1\text{-}3}alkyl\text{-}NR^4$ beingdefined as Q according to claim 1 provided that in the definition of Q, X^2 is $C_{2\text{-}4}alkyl\text{-}NR^4$, in the presence of a suitable amination agent;

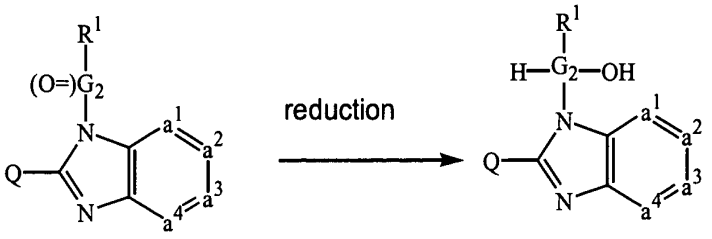
q) deprotecting an intermediate of formula (XXI)



(XXI) (I-q)

with R^1, Q, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and HO-G_1 being defined as G according to claim 1 provided that G is substituted with hydroxy or HO-$(CH_2CH_2O-)_n$; and

r) reducing an intermediate of formula (XXII)



(XXII) (I-q-1)

with R^1, Q, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and H-G_2-OH being defined as G according to claim 1 provided that G is substituted with hydroxy and the carbon atom carrying the hydroxy substituent carries also at least one hydrogen, in the presence of a suitable reducing agent.

[and, if desired, converting compounds of formula (I) into each other following art-known transformations, and further, if desired, converting the compounds of formula (I), into a therapeutically active non-toxic acid addition salt by treatment with an acid, or into a therapeutically active non-toxic base addition salt by treatment with a base, or conversely, converting the acid addition salt form into the free base by treatment with alkali, or converting the base addition salt into the free acid by treatment with acid; and, if desired, preparing stereochemically isomeric forms, metal complexes, quaternary amines or N-oxide forms thereof.]

16. (amended) A product [containing], comprising:

(c) a first compound as [defined] claimed in claim 1; and

(d) a second [another] antiviral compound, [as a combined preparation for simultaneous, separate or sequential use in the treatment or the prevention of viral infections]

wherein said first compound and said second compound are simultaneously, separately or sequentially used in the treatment or the prevention of viral infections.

17. (amended) A pharmaceutical composition, comprising:

(a) a pharmaceutically acceptable carrier; and

(b) as active ingredients:

i. a first compound as claimed in claim 1; and

ii. [another] a second antiviral compound.

Please add the following new claims:

18. (new) The process of claim 15, further comprising the step of converting compound of formula (I'), stereochemically isomeric forms, metal complexes, quaternary amines or *N*-oxide forms thereof, into a therapeutically active non-toxic acid addition salt by treatment with an acid.

19. (new) The process of claim 15, further comprising the step of converting compound of formula (I'), stereochemically isomeric forms, metal complexes, quaternary amines or *N*-oxide forms thereof, into a therapeutically active non-toxic base addition salt by treatment with alkali.

20.(new) The process of claim 15, further comprising the step of converting the acid addition salt form of compound of formula (I'), stereochemically isomeric forms, metal complexes, quaternary amines or *N*-oxide forms thereof, into the free base by treatment with alkali.

21. (new) The process of claim 15, further comprising the step of converting the base addition salt form of compound of formula (I'), stereochemically isomeric forms, metal complexes, quaternary amines or *N*-oxide forms thereof, into the free acid by treatment with acid.